Twirling DNA Rings - Swimming Nanomotors Ready for a Kickstart

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We propose a rotary DNA nanomachine that shows a continuous rotation with a frequency of $10^2 - 10^4$ Hz. This motor consists of a DNA ring whose elastic features are tuned such that it can be externally driven via a periodic temperature change. As a result the ring propels itself through the fluid with a speed up to microns per second.

The long lasting dream of scaling mechanical devices and machines down to the nanoscale (as popularized by R. Feynman [1] and carried on by several visionary groups worldwide [2]) continues to fire the imagination of researchers – now in the third generation. Among many experimental difficulties that appear in this context, choosing the proper material for the assembly of a nanodevice turns out to be crucial. Important material requirements are: stability, self-assembly ability, modularity, replicability, switchability, experimental tractability. Presently one of the most promising materials fulfilling those requirements is DNA [3]. Assemblies based on DNA hybridisation chemistry [4, 5, 6, 7] as well as conformational DNA transitions [8] were successfully exploited to generate periodically switchable nanodevices. However, despite their beauty and conceptual originality all of these devices suffer one major problem: the large kinetic barriers involved in the switching process boost their switching time per cycle to $\sim 10^3$ s, four orders of magnitude slower than their natural counterparts (biological molecular motors). A natural question arises then: Can one achieve *subsecond* switching times with a DNA nanodevice? Can such a device be operated in some manner to *swim directionally and faster than* 1μm/s? In this letter we show theoretically the principal feasibility of such DNA nanomachines.

Let us in the following propose a surprisingly simple nanomotor: a DNA miniplasmid, cf. Fig. 1(a). We will show that despite its structural simplicity a miniplasmid can be turned into a nanomachine able to produce fN forces and self-propelling at speeds of several microns per second through the fluid. In order to run the plasmid as a motor we use here the Euler-angle ψ (cf. Fig. 1(a)) as the relevant degree of freedom [9]. The main idea now is to induce a directed current $\langle \dot{\psi} \rangle$ – in a manner similar to the rotation of a closed rubber tube around its central circular axis – via non-equilibrium fluctuations and the ratchet effect [10, 11], cf. Fig. 1(b). As a result the twirling ring generates a hydrodynamic flowfield (shown in Fig. 1(c)) that remarkably induces an efficient self-propulsion of the motor as detailed below.

The elastic distortion energy of a DNA ring with radius R parametrized by the arc length parameter s will in general be described by three Euler angles $\theta(s)$, $\phi(s)$ and
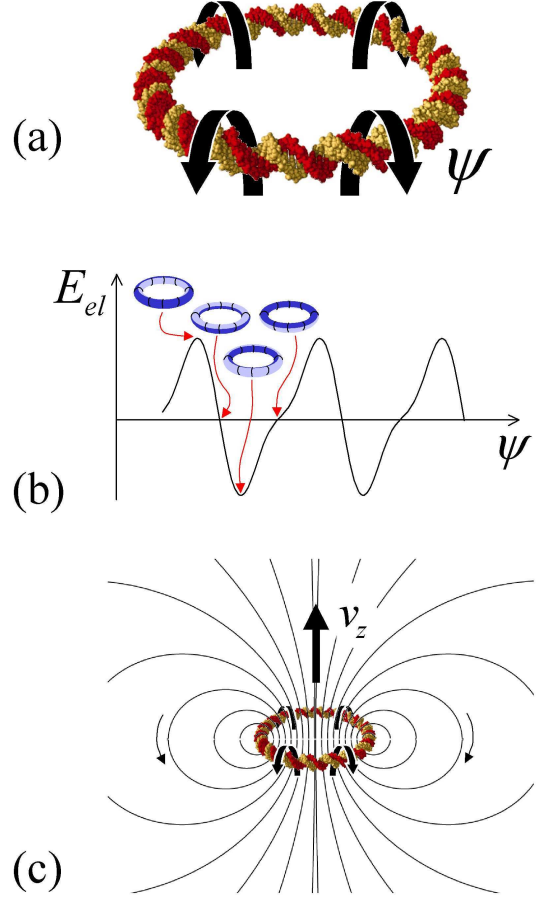

FIG. 1: The operation principle of the DNA-minicircle propeller: (a) The twirling degree of freedom. (b) The elastic energy as a ratchet potential. (c) The flowfield around the twirling ring induces its translational velocity v_z.

$\psi(s)$ via $E_{el} = \frac{1}{2} k_B T \int_0^{2\pi R} \sum_{i=1,2,3} l_i (\omega_i - \kappa_i)^2 ds$ with $\omega_1 = \phi' \sin\theta \sin\psi + \theta' \cos\psi$, $\omega_2 = \phi' \sin\theta \cos\psi - \theta' \sin\psi$ and $\omega_3 = \phi' \cos\theta + \psi'$ [12]. Here l_1 and l_2 are the two principal bending persistence lengths and κ_1 and κ_2 are intrinsic curvatures in two corresponding perpendicular directions. l_3 denotes the twist persistence length and – for simplicity – we choose $\kappa_3 = 0$. The parameters κ_i and l_i reflect the anisotropic bendability as well as intrinsic bendedness of the plasmid; here for sim-
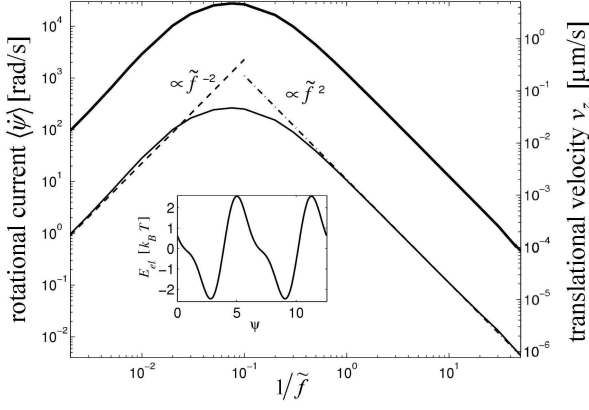
FIG. 2: The rotational current $\langle \dot{\psi} \rangle$ and the induced translational velocity v_z as a function of the dimensionless frequency $\tilde{f}$ of the temperature (potential) oscillations. The DNA ring has the following parameters: $R = 10 nm$, $r_0 = 1 nm$ (typical DNA minicircle), $l_1 = 45$ nm, $l_2 = 50$ nm, $\kappa_1 = \kappa_2 = (200 nm)^{-1}$ leading to the ratchet potential displayed in the inset. Displayed are the asymptotic expressions, Eqs. 5 (dashed line) and 6 (dashed-dotted line) together with the numerical solution of Eq. 2 (thin line) for a temperature ratchet with $A_T = 0.03$. The thick solid line corresponds to an oscillating potential ratchet with $A_E = 0.3$. See text for details.

plicity we assume them to be independent of the arc-length throughout the molecule (e.g. for a 10 basepair (bp) periodic sequence). For the case of DNA mini-circles of short length ($2\pi R \lesssim l_i$) and with constant κ_i and l_i fulfilling the weak bending anisotropy condition $\max \{|l_1 - l_2|/R, l_1\kappa_1, l_2\kappa_2\} \ll l_3/R$ only the conformations close to the circular untwisted state will contribute, i.e., those close to $\theta(s) = \pi/2$, $\phi(s) = s/R$ and $\psi(s) = const$. This leads then to the required ratchet potential acting on ψ:

$$\frac{E_{el}(\psi)}{\pi k_B T} = \frac{l_1 - l_2}{2R}\cos(2\psi) + 2l_1\kappa_1\cos\psi - 2l_2\kappa_2\sin\psi \quad (1)$$

From Eq. 1 we see that for generating a ratchet potential we need both nonzero bending anisotropy, $l_1 - l_2 \neq 0$, as well as non-vanishing intrinsic curvatures, $\kappa_{1,2} \neq 0$. The inset in Fig. 2 demonstrates that reasonable small values of anisotropy and intrinsic curvature can induce a well-defined ratchet potential.

The Fokker-Planck equation describing the time evolution of the probability density $P(\psi, t)$ of the Euler angle ψ writes

$$\zeta\frac{\partial P}{\partial t} = \frac{\partial}{\partial \psi}\left(\frac{\partial E_{el}}{\partial \psi}P + k_B T\frac{\partial P}{\partial \psi}\right) \quad (2)$$

with the friction constant ζ that we will compute below. As a source of non-equilibrium we will choose here a time-dependent variation of temperature $T(t)$, cf. Ref. [13].

Before we compute the friction constant ζ we need to shed some light on the low Reynolds number hydrodynamics of the twirling DNA ring. The latter turns out to

be peculiarly related to the inviscid (ideal) fluid vortices (rings of smoke) and as a matter of fact both of them propagate in analogous manner. To see this we first remark that for a reasonable ring radius $R = 10$ nm (a typical miniplasmid of ≈ 200 bp) and the DNA helix radius $r_0 = 1$ nm the slender body approximation [14] is valid with the slenderness paramenter $\varepsilon = r_0/R = 0.1$. In the spirit of the slender body theory one approximates the flow-field around the twirling ring by superimposing rotlets [15] $\mathbf{u}_{rot}(\mathbf{x}; s) = \Gamma\frac{d\mathbf{c}(s)}{ds} \times (\mathbf{x} - \mathbf{c}(s))/|\mathbf{c}(s) - \mathbf{x}|^3$ placed along the ring centerline $\mathbf{c}(s)$ with arclength parameter s. The rotlet strength $\Gamma = \frac{1}{2}\omega_\mathbf{c}r_0^2$ is given in terms of the angular velocity $\omega_\mathbf{c}$ of the ring about $\mathbf{c}(s)$. The full velocity profile is then given by $\mathbf{u}(\mathbf{x}) = \int_0^{2\pi R} \mathbf{u}_{rot}(\mathbf{x}; s)\,ds$; cf. also the stream lines around the rotating ring shown in Fig. 1(c). When integrating $\mathbf{u}(\mathbf{x})$ over the DNA ring (slender torus) surface in the limit of small r_0/R one obtains a net translational velocity in the z-direction:

$$v_z(\omega_\mathbf{c}) = \frac{r_0^2}{2R}\left(\ln\left(8\frac{R}{r_0}\right) - \frac{1}{2}\right)\omega_\mathbf{c} \quad (3)$$

The fact that Eq. 3 coincides with the well known expression from ideal flow vortex theory [16] should not surprise if we recall that a rotlet $\mathbf{u}_{rot}(\mathbf{x}; s)$ is nothing else but the expression for the velocity field of an ideal point vortex. But despite this kinematic analogy between the twirling DNA and an ideal vortex ring, dynamically they are quite different. The propagation of an ideal vortex ring does not require any external forces/torques and is governed by conservation of kinetic energy and momentum. In sharp contrast to that the low Reynolds-number (Stokes) flow is governed by dissipation and the motion of twirling DNA ring requires the action of a torque $N_\mathbf{c} = 8\pi^2 x_0^2\eta R\omega_\mathbf{c}$ ($\eta = 10^{-3}$ Pa s, the water viscosity) about the central axis $\mathbf{c}$. The latter expression can be verified by integrating the tangential stresses generated by $\mathbf{u}(\mathbf{x})$ over the ring surface. More generally by virtue of the linearity of the Stokes equations we can derive a resistance matrix (M_{kl}) relating the angular velocity $\omega_\mathbf{c}$ (about the circular axis $\mathbf{c}$) and velocity v_z (in the z-direction) with the corresponding external torque $N_\mathbf{c}$ and force F_z:

$$\begin{pmatrix} F_z \\ N_\mathbf{c} \end{pmatrix} = 4\pi^2\eta\begin{pmatrix} M_{11} & M_{12} \\ M_{21} & M_{22} \end{pmatrix}\begin{pmatrix} v_z \\ \omega_\mathbf{c} \end{pmatrix} \quad (4)$$

Combining the previous expressions obtained for $v_z(\omega_\mathbf{c})$ and $N_\mathbf{c}(\omega_\mathbf{c})$ ($F_z = 0$) together with the result of Johnson and Wu [14] for the drag on a rigid slender torus we obtain entries in the leading order: $M_{11} = 2R(\ln 8/\varepsilon + 1/2)^{-1}$, $M_{22} = 2r_0^2 R$ and $M_{12} = M_{21} = r_0^2(\ln 8/\varepsilon - 1/2)(\ln 8/\varepsilon + 1/2)^{-1}$. Note that the symmetry of the resistance matrix being a general feature of swimmers in the Stokes flow [17] provides a good check for the consistency of the involved calculations. Having

the mobility relation 4 one can consider different types of motion, e.g.: (i) The ring is twirling freely ($N_\mathbf{c} = 0$) and moving under the force F_z (or at fixed v_z). (ii) The ring is prevented from rotation ($\omega_\mathbf{c} = 0$) and moved by the force F_z (or at fixed v_z). (iii) The ring is held in position ($v_z = 0$) by imposing a force F_z counterbalancing the action of torque $N_\mathbf{c}$. (iv) The DNA ring is free to move (no external force applied, $F_z = 0$) under an externally imposed torque $N_\mathbf{c}$ (or at given $\omega_\mathbf{c}$). Comparing, for instance, the velocities $v_z^{(i)}$ and $v_z^{(ii)}$ from cases (i) and (ii) one sees that $v_z^{(i)}/v_z^{(ii)} - 1 = M_{12}^2/\det M_{kl} \sim (\varepsilon/2)^2 \ln(8/\varepsilon)$; i.e., a ring with an isotropic DNA sequence (able of twirling) settles faster than a ring with very high barriers to twirling ($\omega_\mathbf{c} = 0$), though in practice the difference is negligible, for instance $\sim 1\%$ for $\varepsilon = 0.1$. By comparing cases (iii) and (iv) we conclude that a ring twirling at fixed $\omega_\mathbf{c}$ and forced not to translate requires a slightly larger torque $N_\mathbf{c}^{iii}(\omega_\mathbf{c})$ than the unconstrained freely translating ring with $N_\mathbf{c}^{iv}(\omega_\mathbf{c})$. However the relative difference is again small and of order $O\left(\varepsilon^2 \ln(8/\varepsilon)\right)$. Therefore by dropping this marginal correction to the leading order we obtain in both cases (iii) and (iv) the angular friction constant $\zeta = N_\mathbf{c}(\omega_\mathbf{c})/\omega_\mathbf{c} \approx 8\pi^2\eta r_0^2 R$, the quantity that appeared above in Eq. 2. Note that the latter is the same (in our $\varepsilon \ll 1$ leading order expansion) as for a straight cylinder with radius r_0 and length $2\pi R$. Finally another interesting feature that can be read off Eq. 4 is the efficiency of the twirling ring propulsion. The latter is independent of the mechanism of twirling and can be defined as the ratio of the power $P_0 = 2\pi^2\eta M_{11}v_z^2$ dissipated by a (for simplicity) rigid ring directly moved by a force as compared to the power $P_{twirl} = \frac{1}{2}N_\mathbf{c}\omega_\mathbf{c}$ dissipated by twirling propulsion at the same translational speed. For a ring with $R = 10$ nm we have $P_0/P_{twirl} \approx 0.8\%$ which is comparable to the efficiency of bacterial propulsion by a rotating flagellum [17].

Having determined the friction constant ζ we return to the ratchet dynamics given by Eq. 2 with the twirling potential Eq. 1. To obtain the directed twirling frequency $\omega_\mathbf{c} := \langle\dot\psi\rangle = -\frac{1}{\zeta}\langle\frac{\partial E_{el}}{\partial\psi}P + k_BT\frac{\partial P}{\partial\psi}\rangle$ we follow Ref. [13] by choosing a periodic time dependent temperature variation as follows: $T(t) = T_0[1 + A_T\sin(2\pi f_T t)]$ with T_0 the mean temperature, A_T the relative amplitude and f_T the frequency of the temperature oscillation. For the case of f_T sufficiently larger than the inverse of the characteristic relaxation time $\tau_0 = 4\pi^2\zeta/(k_BT_0)$ of the twirling degree of freedom (but still much smaller than the frequency of average thermal molecular kicks) an $1/f_T$ asymptotic expansion for the current $\langle\dot\psi\rangle$ can be employed [18]. After a long calculation we obtain (for $f_T > f_{res}$) $\langle\dot\psi\rangle$ up to terms of order $O\left(f_T^{-3}\right)$:

$$\langle\dot\psi\rangle = \frac{12\pi^3 A_T^2 (k_BT_0)^3 l_1 l_2 \kappa_1 \kappa_2 (l_2 - l_1)/R}{f_T^2 \zeta^3 \int_0^{2\pi} d\psi\, e^{-\frac{E_{el}(\psi)}{k_BT}} \int_0^{2\pi} d\psi\, e^{\frac{E_{el}(\psi)}{k_BT}}} \quad (5)$$

From Eq. 5 we see that for an isotropically bendable DNA sequence ($l_2 = l_1$) the directed current vanishes. The same is true if the intrinsic curvature direction coincides with one of the principal axes (i.e. if κ_1 or κ_2 vanish). Both observations are intuitive as in either case the ratchet potential, Eq. 1, becomes left-right symmetric and the ratchet effect disappears.

The low frequency adiabatic limit is obtained from the asymptotic expansion of $P(\tilde\psi, \tilde t)$ ($\tilde\psi = \psi/2\pi$, $\tilde t = t/\tau_0$) for small parameter $\tilde f = f_T\tau_0$, i.e., $P \approx P_0 + \tilde f P_1 + \tilde f^2 P_2$. Rather involved calculations lead to [19]

$$\left\langle\dot\psi\right\rangle = -\frac{\tilde f^2}{\tau_0}\int_0^1 d\tilde t\, \overline{\frac{1}{\overline{F}}}\overline{F\partial_{\tilde t}\vec{P_1}} \quad (6)$$

with $E(\tilde\psi, \tilde t) = F(\tilde\psi, \tilde t)^{-1} = e^{-E_{el}(\tilde\psi)/k_BT(\tilde t)}$ and the abbreviations $\overrightarrow{(...)}$ and $\overline{(...)}$ defined as in [18] but with the integrations with respect to $\tilde\psi$. Furthermore the density distributions P_0 and P_1 from the upper expansion are given by $P_0 = E/\overline{E}$ (Boltzmann distribution in the adiabatic limit) and $P_1 = \frac{T_0}{T}E\left(\overrightarrow{Fc_1} - \frac{1}{\overline{E}}\overline{E\overrightarrow{Fc_1}}\right)$ with $c_1 = \overrightarrow{\partial_{\tilde t}P_0} - \frac{1}{\overline{F}}\overline{F\overrightarrow{\partial_{\tilde t}P_0}}$.

Equations 5 and 6 together with Eq. 1 and $\zeta = 8\pi^2\eta r_0^2 R$ allows us to get the twirling speed $\omega_\mathbf{c} = \langle\dot\psi\rangle$ and by virtue of Eq. 3 the induced translational velocity $v_z(\omega_\mathbf{c})$ for arbitrary DNA elastic parameters $l_{i=1,2}$ and $\kappa_{i=1,2}$.

How fast can we operate the twirling ring machine? We shall assume some realistic parameter values for the DNA ring: $R = 10$ nm, $r_0 = 1$ nm (typical DNA minicircle) leading to $\zeta = 2\cdot 10^{-7}k_BT$s. Furthermore we set $l_1 = 45$ nm, $l_2 = 50$ nm, $\kappa_1 = \kappa_2 = (200\text{nm})^{-1}$ which corresponds to a rather modest anisotropy and intrinsic curvature. For the temperature variation amplitude we choose $\Delta T = \pm 10$ K, i.e., $A_T \approx 1/30$ (at room temperature $T_0 = 300$ K). Figure 2 provides a log-log plot of the rotational current and the corresponding drift speed of the ring as a function of the dimensionless frequency $\tilde f$ of the temperature variation. The thin solid curve gives the numerical result obtained from Eq. 2, the two straight lines correspond to the analytical results for the two asymptotic cases, Eqs. 5 and 6. As can be seen from this plot the two limits show a $\tilde f^{-2}$ and $\tilde f^2$ dependence, respectively, in accordance with Eqs. 5 and 6. The maximal rotational current is achieved in the crossover region, namely $\omega_\mathbf{c} \approx 200$rad/s for $\tilde f \approx 10^{-1}$. Following Eq. 3 this implies a translational velocity of $v_z = 50$nm/s.

Such fast temperature oscillations are technically feasible and might be most conveniently generated by adiabatic pressure variations e.g. by ultrasound. Another promising method is to use the inductive heating of metal nanocrystals that are covalently attached to the DNA ring. In fact, this method has been successfully used to control the hybridization behavior of DNA [20]. This might also point towards an alternative way of driving the ratchet, namely via a periodic

variation of the elastic properties of the ring. Operating the system close to the DNA duplex melting temperature is likely to induce strong oscillations in the overall ring stiffness. The thick solid line in Fig. 2 shows the rotational current obtained when the elastic energy is varied as $\tilde{E}_{el}(\psi, t) = E_{el}(\psi)(1 + A_E \sin(2\pi f_E t))$ where we chose the relative amplitude $A_E = 0.3$. As can be seen from Fig. 2 the maximal current of this oscillating potential ratchet occurs roughly at the same frequency as that of the thermal ratchet but the value of $\omega_{\mathbf{c}}$ is much higher, namely on the order of $2 \times 10^4 \text{rad/s}$ which implies a quite notable translational velocity of $v_z = 5\mu\text{m/s}$. As a comparison a typical bacterium moves at $30\mu\text{m/s}$. Our ring ratchet (with oscillating potential) resembles in many respects "real" biological nanomotors. Besides its nanoscopic size (radius 10 nm), swimming efficiency (0.8%) and speed ($4\mu\text{m/s}$) it can generate forces and torques close to that of biomolecular motors. Although the net translational force resulting from Eq. 4 $F_z = 4\pi^2 \eta M_{12}\omega_{\mathbf{c}} \approx 0.6$ fN is comparably small (due to cancelling of most of the stresses), the local torque $N_{\mathbf{c}} = 8\pi^2 \eta r_0^2 R \omega_{\mathbf{c}} \approx 0.004 k_B T$ and the force acting at the DNA surface $F_{loc} = N_{\mathbf{c}}/r_0 = \zeta \omega_{\mathbf{c}}/r_0 \approx 16$ fN are significant if we consider the simplicity of the mechanism behind.

From an experimental point of view one should be aware of the fact that a ring (twirling or non-twirling) looses its initial orientation almost instantaneously due to rotational diffusion. The typical relaxation time scale of this process is on the order $\eta R^3/(k_B T)$ (up to logarithmic corrections [21]) which for a ring with $R = 10$ nm leads to 10^{-7} s. That means that a single twirling ring in solution will not perform any noticeable translational drift. A possible solution to the problem is to put the ring on a "track", e.g. to thread it on a straight DNA chain. Another promising direction is to prepare a semi-dilute solution of such rings and then study their response due to an induced twirling. The resulting hydrodynamic flow can lead to an attraction between the rings that might facilitate interesting collective behavior of the nanomotors like the formation of columns of twirling rings that drive a solvent flow through the resulting channel.

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